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10/774,928	02/09/2004	Jose A. O'Daly	299 P 010	8743

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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/774,928	O'DALY, JOSE A.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 27(part b), 29, 30 (part b), 32, 33 (part b), 35, 36 (part ii a, ii b and ii c), and 38.

Continuation of Disposition of Claims: Claims rejected are 1, 2, 21, 22, 23-26, 27(a), 28, 30(a), 31, 33(a), 34, 36 (part (a)(i)-c (i)) and 37 .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse in the reply filed on 6/22/06 is acknowledged. Applicants indicated that it was impossible to elect a restricted Group for examination, but have elected the following Species: Species A: a 73kDA protein comprising SEQ ID Nos: 1, 5 and 6; SPECIES C: an 80kDa protein comprising SEQ ID Nos: 1, 3 and 4, and SPECIES E: an 82kDa protein comprising SEQ ID Nos: 1 and 2. The traversal of the Restriction Requirement is on the ground(s) that the immunogenic polypeptides of 73, 80, and 82-kDa molecular weight are to be combined and used together. This is found persuasive and the former Restriction Requirement, which separated the invention into 3 Groups, is hereby withdrawn. However, the species election remains in place. Applicants argue that members of the Markush Group is small and therefore it would not place an undue burden on the Examiner to examine all of the species together. This is not found persuasive because the species are independent or distinct because each of the methods utilize distinct protein products comprising proteins having different primary structures and it would place an undue burden on the Examiner to examine them all together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 2, 21, 22, 23-26, 27(a), 28, 30(a), 31, 33(a), 34, 36 (part (a)(i)-c (i)) and 37 are under examination.

Claims 27(part b), 29, 30 (part b), 32, 33 (part b), 35, 36 (part ii a, ii b and ii c), and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species.

Claim Rejections - 35 USC § 112-2nd paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 2, 21, 22, 23-26, 27(a), 28, 30(a), 31, 33(a), 34, 36 (part (a)(i)-c (i)) and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite due to the phrase "*interferes* with at least one of the following interactions: a CLA and E-selectin interaction ...". It is unclear what is meant by the term 'interferes'. It appears from the disclosure that it is intended to encompass 'an inhibition". Clarification and correction is required.

Claim 1 is also vague and confusing due to the phrase "a human susceptible to symptoms of psoriasis". The specification does not define this group. It is unclear how to determine a group of human susceptible to psoriasis. Is the method intended to abate symptoms of psoriasis in patients already suffering from the disease? Clarification and/or correction is required.

Claims 21, 22, 23-26, 27(a), 28, 30(a), 31, 33(a), 34, 36 (part (a)(i)-c (i)) and 37 are vague and confusing because it is unclear whether the claimed methods intend to use isolated protein and/or mixtures of three isolated proteins or if the agent is a purified

protein extract as claimed in parent application 09/809,003 (now US Patent No. 6,673,351). Claim 21 does not adequately define the agent which is to be used in the claimed methods if the agent is intended to be a purified protein extract because the extract can continually change depending on the method used to isolate it from the killed amastigote cells. Therefore, the metes and bounds of the invention cannot be understood. The extract should be defined as recited in claim 1 of US Patent No. 6,673,351.

Claim Objections

4. It is noted that once the non-elected species are removed from claim 27, the claim will be identical to claim 28. It is noted that once the non-elected species are removed from claim 30, the claim will be identical to claim 31. It is noted that once the non-elected species are removed from claim 33, the claim will be identical to claim 35. It is noted that once the non-elected species are removed from claim 36, the claim will be identical to claim 37. These claims face objection under 37 CFR 1.75 as being substantial duplicate of claims if amendment is not made. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112-Scope of Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 2, 21, 22, 23-26, 27(a), 28, 30(a), 31, 33(a), 34, 36 (part (a)(i)-c (i)) and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "A method for the abatement of clinical symptoms of psoriasis comprising administering a an immunotherapeutic agent comprising a purified protein extract wherein said purified extract is isolated by diethylaminoethyl Sephadex chromatography of a Nonidet P-40 insoluble particulate antigen fraction derived from isolated killed cells of amastigotes from at least one species of the Leishmania genus, said particulate antigen fraction solubilized with 8 M urea and 0.025 M Tris[hydroxymethyl]aminomethane pH 8.3 applied to diethylaminoethyl Sephadex and eluted with a solution comprising 0.1 M. sodium chloride, 8 M urea and 0.025 M. Tris[hydroxymethyl]aminomethane pH 8.3, said purified protein extract consisting of polypeptides having apparent molecular weights after total reduction and alkylation of 73, 80 and 82 kDa", does not reasonably provide enablement for "a method for selectively inhibiting T-cell rolling in a human susceptible to symptoms of psoriasis, the method comprising the step of administering ***[any]*** compound that interferes with at least one of the following interactions: a CLA and E-selectin interaction, a LFA-1/ICAM interaction or a VLA/VACM interaction". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining

whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The claimed method allows for use of a compound of any chemical/structural make-up from any source, including synthetic to selectively inhibit T-cell rolling. The instant specification only teaches and discloses immunotherapeutic compounds comprising purified protein extracts from *Leishmania*; e.g., a purified protein extract wherein said purified extract is isolated by diethylaminoethyl Sephadex chromatography of a Nonidet P-40 insoluble particulate antigen fraction derived from isolated killed cells of amastigotes from at least one species of the Leishmania genus, said particulate antigen fraction solubilized with 8 M urea and 0.025 M Tris[hydroxymethyl]aminomethane pH 8.3 applied to diethylaminoethyl Sephadex and eluted with a solution comprising 0.1 M. sodium chloride, 8 M urea and 0.025 M. Tris[hydroxymethyl]aminomethane pH 8.3, said purified protein extract consisting of polypeptides having apparent molecular weights after total reduction and alkylation of 73, 80 and 82 kDa. The specification teaches that these compositions can result in the abatement of clinical symptoms of psoriasis. However, the specification has not demonstrated which, if any, of the disclosed compositions can 'interfere' with any or all of the following interactions: a CLA and E-selectin interaction, a LFA-1/ICAM interaction or a VLA/VACM interaction. There is no correlation or data showing the administration

of a disclosed compound and the prevention or inhibition of any of those interactions. It is known in the art that psoriasis is a chronic, remitting and relapsing scaly and inflammatory skin disorder of unknown. It is taught in the art that the mechanism of the human immune system that triggers symptoms of psoriasis consists of T-cell lymphocytes. See Journal of the American Academy of Dermatology, 2003. 49: S44-50. Tables 4-9, 11-14, 22 and Examples 14-17 demonstrate the abatement of symptoms of psoriasis using the composition comprising a purified protein extract wherein said purified extract is isolated by diethylaminoethyl Sephadex chromatography of a Nonidet P-40 insoluble particulate antigen fraction derived from isolated killed cells of amastigotes from at least one species of the Leishmania genus, said particulate antigen fraction solubilized with 8 M urea and 0.025 M Tris[hydroxymethyl]aminomethane pH 8.3 applied to diethylaminoethyl Sephadex and eluted with a solution comprising 0.1 M. sodium chloride, 8 M urea and 0.025 M. Tris[hydroxymethyl]aminomethane pH 8.3, said purified protein extract consisting of polypeptides having apparent molecular weights after total reduction and alkylation of 73, 80 and 82 kDa. However, the specification fails to demonstrate that any one immunotherapeutic agent in the specification specifically interfered with at least one of the following interactions: a CLA and E-selectin interaction, a LFA-1/ICAM interaction or a VLA/VACM interaction. No results are provided which correlate the immunotherapeutic agents and the inhibition or blockage of any of these interactions. Accordingly, it would take undue experimentation to make and /or use the invention as claimed.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Pariser, David M. MD. (Managed Care. December 2003. pages 50-56). NOTE: the instant claims only are entitled to a priority filing date of 2/9/04. The instant claims and methods were first presented in this CIP application and the claimed subject matter was not in the grandparent or parent applications, e.g., inhibiting T-cell rolling by inhibiting CLA and E-Selection, etc..).

Pariser teaches the biology behind T-cell homing (rolling) and how it works in patients with psoriasis (see Figure 1 on page 52 and Figure 3 on page 53, as well as disclosure on pages 52-53). Pariser teaches that instead of solely topical treatments the new biologic agents for treating psoriasis are moving in the direction of systemic therapy. See column 2, page 52. The reference teaches the use of the drug, Efalizumab (RAPTIVA™), to inhibit the LFA-1/ICAM-1 reaction which is used in the prior art for the treatment of psoriasis. See top of column 3, page 52. Instant claims 1 and 2 allow the use of *any* compound which interferes with at least one of the following interactions: a CLA and E-selectin interaction, a LFA-1/ICAM interaction or a VLA/VACM interaction. The use of the *Leishmania* compounds described in the specification is not claimed. Efalizumab is an immunostimulant, e.g., a humanized monoclonal antibody.

9. Prior art made of record:

O'Daly et al (Gac Med Caracas, 103(2): 133-177, 1995). O'Daly et al teach a preparation of a vaccine from Leishmania parasite strains, *L.amazonenis, L.venezuelensis, L.brasiliensis, and L.chagasi.* Each parasite was cultivated and was incubated at the particular temperature of transformation into the amastigote form. Once the parasite reached the amastigote stage they were subjected to a medium with an agent effective to kill the parasites. The parasites were harvested by centrifugation and washed. The isolated parasites were treated by incubation with a medium comprising a detergent, which extracts some proteins from the parasite. The proteins in the total extract were further fractionated and purified by centrifugation. Washing repeatedly further refined the centrifugation pellet comprising fractionated particulate isolated proteins; and, the supernatant fraction containing other *Leishmania* proteins was not further used. This centrifugation step is seen as fractionating and purifying the particulate proteins from the detergent extracted proteins and is fact purifying the particulate protein fraction from that solubilized by the detergent medium. The purified/fractionated particulate proteins from the detergent extract were resuspended in medium and then sonicated. The protein content of the extracted sonicate was determined and alumina was added at a concentration of 1mL/mg of protein of each one of the *Leishmania* parasite strains, which were added in equal parts to obtain a final concentration of 1000ug/ml of *Leishmania* antigen. See page 1 of the translation of the article, under "Preparation of vaccine". The process of preparing the *Leishmania* vaccine extract according to O'Daly is substantially the same as that provided for in the

specification at pages 3-4 and pages 11-12. Therefore, the composition of a purified protein extract comprising isolated polypeptides that is used in the claimed method appears to be the same as the compositions of the prior art. The proteins contained therein are in fact extracted/isolated/purified from the total amastigote form of the parasite to the same extent as provided for in the extracts of the specification. The recitation of the partial sequences from the *Leishmania* polypeptides found in the composition of the prior art is merely further characterization of the polypeptides of the prior art composition. The sequences are an inherent property of the composition of the prior art.

However, O'Daly does not teach or suggest that the vaccines/compositions can be used in methods to 'selectively inhibit T-cell rolling in a human susceptible of psoriasis and that the vaccines/compositions interfere with at least one of the following interactions: a CLA and E-selectin interaction, an LFA-1/ICAM interaction or a VLA/VACM interaction'. Therefore, the reference has not been applied to the current claims.

10. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 7:30 AM-6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

8/17/06

Jennifer Graser
Primary Examiner
Art Unit 1645